# ROLE OF SODC PROTEIN IN ANTINEOPLASTIC DRUG RESISTANCE

Burgos-Molina AM[1], Alamilla-Presuel JC[2], González-Vidal A[2], Ruiz-González OM[3], Ruiz-Gómez MJ[2]

[1]Department of Immunology, University of Málaga, Málaga, Spain
[2]Department of Radiology and Physical Medicine, University of Málaga, Málaga, Spain
[3]Superior Technical School of Architecture, University of Málaga, Málaga, Spain

## Introduction

The correct regulation of protein homeostasis, or proteostasis, in cells is vital for the health of organisms. Several studies have shown that improve proteostasis in the endoplasmic reticulum (ER) favors cellular resistance to stress. Others studies have demonstrated that in a cytotoxic stress situation, like chemotherapy, cells are able to increase fundamental mechanisms to survive againts the drug and, thus, acquire resistance. These mechanisms implicate overexpression of proteins that can be used such us predictive biomarkers of drug resistance.

## Objectives

The aim of this work is to evaluate the role of SODC protein in the process of drug resistance.

## Methods

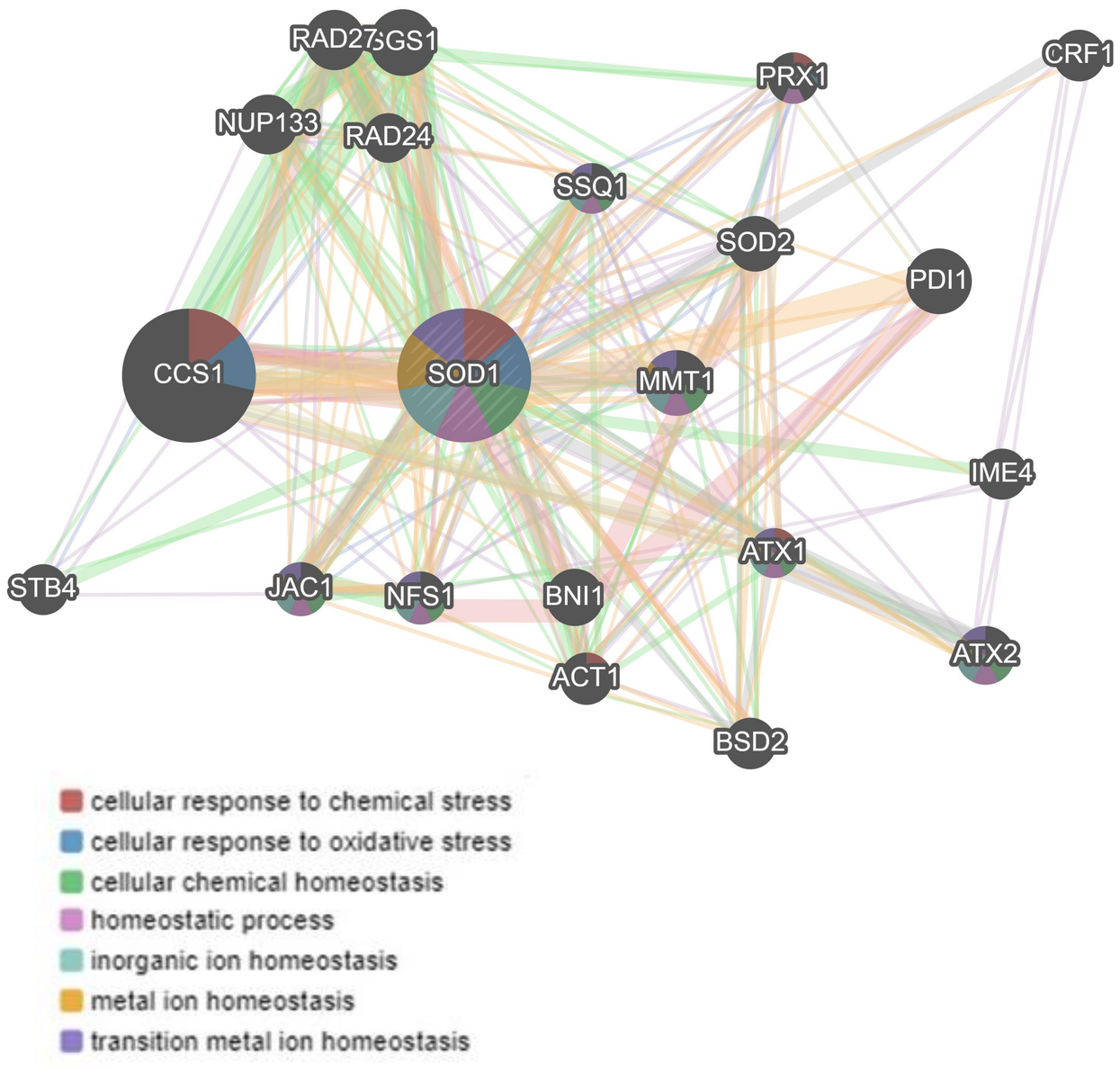
The drug bleomycin was used in the process of resistance acquisition by exposure of S. cerevisiae cells. An extraction, purification and identification of proteins were made by tandem mass spectrometry using an ion trap system. The emPAI value (exponentially modified protein abundance index) was used to study protein expression. Genemania software was used to study genes.

## Conclusions

Cells need homeostasis to survive, therefore, they use the different pathways available to obtain it. The SODC protein overexpression, which is implicated in this process, suggests that could be implicated in the process of acquisition resistance during chemotherapy

## Results

The SODC protein (SOD1 gene) is a cytosolic copper-zinc superoxide dismutase implicated in copper-zinc homeostasis, superoxide metabolism, cellular aging, cell wall organization, regulation of cellular respiration, and transcription regulation in response to oxidative stress. We found an overexpression of this protein of 3,4-fold respect to the wild type strain. For the activation of the bleomycin molecule, the union with a reduced transition metal [Fe (II) or Cu (I)], the presence of oxygen and a reducing agent are necessary. Once activated, the cytotoxic effect is exerted through the generation of ROS and by direct damage to DNA and RNA. Active bleomycin can carry out the production of hydroxyl radicals, superoxide and hydrogen peroxide, which react rapidly and non-specifically with molecules, producing the oxidation of lipids, proteins and nucleic acids. Therefore, the overexpression of this protein is logical since SODC is responsible, on the one hand, for the homeostasis of copper, which is a reduced transition metal necessary for the activation of the bleomycin molecule. On the other hand, it is responsible for the metabolism of superoxide, which catalyzes the dismutation of superoxide into oxygen and hydrogen peroxide. Because of this, it is an important antioxidant defense in most cells. So this fact could entail the use of this protein as new bleomycin resistance biomarker. The homologous gene in humans is SOD1.




***Functions and interactions between genes that encode proteins with ΔemPAI > 2.5 in bleomycin-resistant strain.***